

CLAIMS

We claim:

1. An isolated nucleic acid molecule comprising a polynucleotide having a nucleotide sequence at least 95% identical to a sequence selected from the group consisting of:
 - (a) a polynucleotide fragment of SEQ ID NO:1, 3, or 5, which is hybridizable to SEQ ID NO:1, 3, or 5;
 - (b) a polynucleotide encoding a polypeptide fragment of SEQ ID NO:2, 4, or 6, which is hybridizable to SEQ ID NO:1, 3, or 5;
 - 10 (c) a polynucleotide encoding a polypeptide domain of SEQ ID NO:2, 4, or 6, which is hybridizable to SEQ ID NO:1, 3, or 5;
 - (d) a polynucleotide encoding a polypeptide epitope of SEQ ID NO:2, 4, or 6, which is hybridizable to SEQ ID NO:1, 3, or 5;
 - (e) a polynucleotide encoding a polypeptide of SEQ ID NO:2, 4, or 6, which
15 is hybridizable to SEQ ID NO:1, 3, or 5, having biological activity;
 - (f) a polynucleotide which is a variant of SEQ ID NO:1, 3, or 5;
 - (g) a polynucleotide which is an allelic variant of SEQ ID NO:1, 3, or 5;
 - (h) a polynucleotide which encodes a species homologue of the SEQ ID NO:2, 4, or 6;
 - 20 (i) a polynucleotide which represents the complimentary sequence (antisense) of SEQ ID NO:1, 3, or 5;
 - (j) a polynucleotide which encodes the mature form of SEQ ID NO:1, 3, or 5;
 - (k) a polynucleotide capable of hybridizing under stringent conditions to any one of the polynucleotides specified in (a)-(k), wherein said polynucleotide does not
25 hybridize under stringent conditions to a nucleic acid molecule having a nucleotide sequence of only A residues or of only T residues.
2. The nucleic acid sequence of claim 1 comprising all or a portion of the nucleic acid sequence as shown in SEQ ID NO:1, 3, or 5.
3. An expression vector comprising a nucleic acid molecule as claimed in
30 claim 1 and an expression control sequence operatively linked to the nucleic acid molecule.

4. A transformant host cell including an expression vector comprising a nucleic acid molecule as claimed in claim 1 and an expression control sequence operatively linked to the nucleic acid molecule.

5. A purified and isolated nucleic acid sequence comprising the complement of the nucleic acid sequence of claim 1

6. A tumor necrosis factor molecule comprising the amino acid sequence as shown in SEQ ID NO:2, 4, or 6.

7. A method of producing a tumor necrosis factor molecule, said method comprising the steps of:

10 a) inserting a nucleic acid sequence according to claim 1 encoding said tumor necrosis factor molecule into an appropriate expression vector,

b) transfecting said expression vector into an appropriate transfection host cell,

15 c) growing said transfected host cells in an appropriate culture media, and

d) purifying the tumor necrosis factor molecule from said culture media.

8. An isolated nucleic acid sequence which hybridizes under stringent conditions to the nucleic acid sequence of claim 2.

20 9. An antibody specific for the tumor necrosis factor molecule as claimed in claim 6.

10. The antibody of claim 9 wherein said antibody is a monoclonal antibody.

11. The tumor necrosis factor molecule of claim 6, produced by:

25 a) inserting a nucleic acid sequence encoding said tumor necrosis factor molecule into an appropriate expression vector,

b) transfecting said expression vector into an appropriate transfection host cell,

30 c) growing said transfected host cells in an appropriate culture media, and

d) purifying the tumor necrosis factor molecule from said culture media.

12. A method for identifying a receptor which is capable of binding to the tumor necrosis factor molecule of claim 6, or to a part of said tumor necrosis factor molecule, said method comprising the steps of:

5 (a) reacting said tumor necrosis factor molecule, or part of said tumor necrosis factor molecule, with said receptor which potentially is capable of binding the tumor necrosis factor molecule or part of said tumor necrosis factor molecule, under conditions which permit the formation of receptor-tumor necrosis factor molecule complexes; and

10 (b) assaying for receptor-tumor necrosis factor molecule complexes, for free tumor necrosis factor molecule, for non-complexed receptor, or for activation of the receptor.

13. A transgenic insect that misexpresses a nucleic acid of claim 1.

14. The nucleic acid of claim 2 comprising nucleotides 652 to 1878 of SEQ ID NO:1.

15 15. A nucleic acid sequence that hybridizes under conditions of high stringency to the nucleic acid sequence of claim 14.

16. An expression vector comprising a nucleic acid molecule as claimed in claim 15.

17. A transformant host cell including an expression vector of claim 16.

20 18. The nucleic acid of claim 2 comprising nucleotides 1 to 1218 of SEQ ID NO:3.

19. A nucleic acid sequence that hybridizes under conditions of high stringency to the nucleic acid sequence of claim 18.

20. An expression vector comprising a nucleic acid molecule as claimed in claim 19.

21. A transformant host cell including an expression vector of claim 20.

22. The nucleic acid of claim 2 comprising nucleotides 634 to 1860 of SEQ ID NO:5.

23. A nucleic acid sequence that hybridizes under conditions of high stringency to the nucleic acid sequence of claim 22.

24. An expression vector comprising a nucleic acid molecule as claimed in claim 23.

25. A transformant host cell including an expression vector of claim 24.
26. The isolated nucleic acid molecule of claim 2, wherein the nucleotide sequence comprises sequential nucleotide deletions from either the C-terminus or the N-terminus.
- 5 27. The isolated polypeptide of claim 11, wherein the the full length protein comprises sequential amino acid deletions from either the C-terminus or the N-terminus.
28. An isolated antibody that binds specifically to the isolated polypeptide of claim 11.
- 10 29. A recombinant host cell that expresses the isolated polypeptide of claim 11.
30. An isolated polypeptide comprising an amino acid sequence at least 95% identical to a sequence selected from the group consisting of:
- 15 (a) a polypeptide fragment of SEQ ID NO:2, 4, or 6;
- (b) a polypeptide fragment of SEQ ID NO: 2, 4, or 6, having biological activity;
- (c) a polypeptide domain of SEQ ID NO: 2, 4, or 6;
- (d) a polypeptide epitope of SEQ ID NO: 2, 4, or 6;
- (e) a full length protein of SEQ ID NO: 2, 4, or 6;
- 20 (f) a variant of SEQ ID NO: 2, 4, 6;
- (g) an allelic variant of SEQ ID NO: 2, 4, 6; or
- (h) a species homologue of SEQ ID NO: 2, 4, 6.
- (i) A mature protein of SEQ ID NO:2, 4, or 6.
- 25 31. The isolated polypeptide of claim 30, wherein the the full length protein comprises sequential amino acid deletions from either the C-terminus or the N-terminus.
32. An isolated antibody that binds specifically to the isolated polypeptide of claim 30.
- 30 33. A recombinant host cell that expresses the isolated polypeptide of claim 30.

34. A tumor necrosis factor molecule comprising amino acid 53 to 409 of SEQ ID NO:2.
35. A tumor necrosis factor molecule comprising amino acid 53 to 406 of SEQ ID NO:4.
- 5 36. A tumor necrosis factor molecule comprising amino acid 53 to 409 of SEQ ID NO:6.
37. An isolated antibody that binds specifically to the isolated polypeptide of claim 34.
38. A recombinant host cell that expresses the isolated polypeptide of claim 34.
- 10 39. A method of identifying a receptor of claim 12 wherein the receptor is a polypeptide.
40. A method of identifying a receptor of claim 12 wherein the receptor is a small molecule.
- 15

Add B2